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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/089,986	Applicant(s) Kurosawa et al.
	Examiner Rebecca Prouty	Art Unit 1652

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 12-29 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 12-29 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2,8
4) ☐ Interview Summary (PTO-413) Paper No(s). ____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 1-11 have been canceled. Claims 12-29 are at issue and are present for examination.

Claims 12-13, 20, 21, 23, 24, 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of DNA molecules encoding any protein that regenerates luciferin from oxyluciferin and D-cysteine wherein said protein is from any source (Claims 12, 13, 20, 21, 23, 24, 26, and 27), from a luminescent organism (Claim 13), from *Coleoptera* (Claim 14), or from a firefly (Claims 15-17). The specification teaches the structure of only a single representative species of such DNAs. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding a protein that regenerates luciferin from oxyluciferin and D-cysteine. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a

skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 12-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding the protein of SEQ ID NO:2, does not reasonably provide enablement for any polynucleotide encoding any protein that regenerates luciferin from oxyluciferin and D-cysteine, any firefly protein that regenerates luciferin from oxyluciferin and D-cysteine or any protein 50% homologous to SEQ ID NO:2 that regenerates luciferin from oxyluciferin and D-cysteine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 12-23 are so broad as to encompass any polynucleotide encoding any protein that regenerates luciferin from oxyluciferin and D-cysteine (Claims 12, 18, 20, 21, 23, 24, 26 and 27), wherein said protein is from a luminescent organism (Claim 13), from *Coleoptera* (Claim 14), or from a firefly (Claims 15-17) or any protein 50% homologous to SEQ ID NO:2 that regenerates luciferin from oxyluciferin and D-cysteine (Claims 19, 22, 25, and 27). The scope of the claims is not commensurate with the

enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and skilled knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid and encoding nucleic acid sequences of a single protein, i.e., SEQ ID NO:2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in a given protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any conservative to modification for a given protein to diminish

with [illegible]th further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any polynucleotide encoding any protein that regenerates luciferin from oxyluciferin and D-cysteine, any firefly protein that regenerates luciferin from oxyluciferin and D-cysteine or any protein 50% homologous to SEQ ID NO:2 that regenerates luciferin from oxyluciferin and D-cysteine. because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting luciferin regenerating activity; (B) the general tolerance of luciferin regenerating proteins to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polynucleotide encoding any protein that regenerates luciferin from oxyluciferin and D-

cysteine, any firefly protein that regenerates luciferin from oxyluciferin and D-cysteine or any protein 50% homologous to SEQ ID NO:2 that regenerates luciferin from oxyluciferin and D-cysteine. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel vectors/organisms, i.e., *Escherichia coli* JM109(pLRE) FERM BP6908. Since the vectors are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmids' sequences are not fully disclosed, nor have all the

sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the plasmids. The specification does not disclose a repeatable process to obtain the vectors and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of these plasmids should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that applicants have deposited the organisms but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. During the pendency of this application , access to the invention will be afforded to the Commissioner upon request;
2. All restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
3. The deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
4. The deposit will be replaced if it should ever become inviable.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13-18, 20, 21, 23, 24, 26, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kajiyama (US Patent 5,714,5[illegible]).

Kajiyama discloses an enzyme from fireflies which regenerates luciferin from oxyluciferin and D-cysteine. They teach the isolation of this protein from North American fireflies (i.e., *Photinus pyralis)* and Japanese fireflies (i.e., *Luciola cruciata* and *Luciola lateralis)*. The many advantages of recombinant production of useful proteins are well known within the art as are recombinant methods of obtaining the necessary genes. These advantages include the ability to produce much

larger quantities of the protein, being able to produce the protein in more easily handled organisms, reducing the number of steps necessary for the purification of a protein and producing the protein in a purer form by using an organism that does not include naturally occurring contaminants of the protein. As such the disclosure of a useful protein, such as that of Kajiyama clearly suggests to the ordinary skilled artisan a gene encoding for the protein as such a gene would be useful to produce large quantities of the protein. Therefore, it would have been obvious to one of ordinary skill in the art to isolate and express the gene encoding the luciferin regenerating protein disclosed by Kajiyama using well known recombinant methods for the isolation of such genes, insertion of the isolated gene into an expression vector, transformation into a suitable host and expression of the encoded protein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652